REMARKS

Claims 24-27, 29 and 32-36 were pending in the application.

Claims 25 and 32-36 were cancelled without prejudice to presentation in related applications.

Claims 24 and 27 were amended to further clarify the claimed invention. Claim 24 was also amended to recite a functional feature of the claimed sequences, support for which can be found throughout the application as filed including, for example, in paragraphs [0032], [0037], [0091] and [0195]. New claim 37 was added, reciting an additional functional limitation. Applicants note that at the time of filing it was well-known that Egr1 (early growth response gene 1) is a transcription factor and binds to the promoter of the inosine-5'monophosphate dehydrogenase type II gene (see, for example, the Eid *et al* reference and the Monia patent cited by the Office (US Patent 6,008,048, column 1).

No new matter has been added.

Upon entry of this amendment, claims 24, 26, 27, 29 and 37 will be pending.

Withdrawn Rejections

Applicants note with appreciation the withdrawal of the rejections of claims 24-27 and 29 under 35 U.S.C. §112, second paragraph, for the recitation of the phrases "of an unaffected individual", "the level of mRNA in (a)", "a level of the mRNA in a second sample", and "a level of the mRNA in a third sample", and of claims 24-27 and 29 under 35 U.S.C. §102(b)

Rejections under 35 U.S.C. §112, second paragraph

Claims 24-31 remain rejected under 35 U.S.C.§112, second paragraph. The Office alleges that with respect to the recitation in the rejected claims of the phrase "... a decrease of at least 50% [100% in claim 29] between the level of the nucleotide sequence in (a) and the level of the nucleotide sequence in the sample indicates that the patient has colon cancer" that it is "unclear whether colon cancer tissue exhibits decreased expression of SEQ ID NO:167

nucleotide as compared to normal colon tissue or whether normal colon tissue exhibits decreased expression of SEQ ID NO:167 nucleotide as compared to colon cancer tissue expression constitutes a 50% decrease." Applicants do not agree.

As set forth in Applicants' previous response, one of skill in the art would readily understand that a patient is diagnosed as having colon cancer when tissue exhibits decreased expression of SEQ ID NO:167 nucleotide less by at least 50% than the expression of SEQ ID NO:167 nucleotide in normal colon tissue. As suggested by the Examiner in a recent telephone conference and in an attempt to advance the prosecution of the pending claims to allowance, Applicants have amended claims 24, 27 and 29 to further clarify that decreased expression of SEQ ID NO:167 nucleotide in a patient sample (as compared to the level of expression of SEQ ID NO:167 nucleotide in normal colon tissue) indicates that the patient has colon cancer.

In view of the foregoing, Applicants respectfully request the withdrawal of the rejections under 35 U.S.C. §112, second paragraph.

Rejections under 35 U.S.C. §112, first paragraph (enablement)

Claims 24-27 and 29 and new claims 32-36 were rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the enablement requirement. The Office acknowledges that the claims are enabled:

> for a method of diagnosing prostate cancer comprising determining the level of a nucleotide sequence comprising SEQ ID NO:167 in a patient sample ... and comparing said level to the level of nucleotide sequence comprising SEQ ID NO:167 in non-cancerous prostate tissue, wherein a decreased level of nucleotide sequence comprising SEQ ID NO:167 in the non-cancerous prostate tissue as compared to the patient sample indicates that the patient has prostate cancer ...".

However, the Office alleges that the specification is not enabled for methods of diagnosing colon cancer, methods for diagnosing prostate cancer (by comparing patient samples to "non-cancerous colon tissue samples"), or methods for diagnosing prostate cancer (by comparing patient samples

to "non-cancerous prostate samples"). (Office Action, page 7, underlining in original). Applicants do not agree.

Preliminarily, Applicants note that claims 25 and 32-36 were cancelled without prejudice, rendering the rejections moot to the extent they refer to such claims. Claims 24 and 27 were amended to recite that decreased expression in the patient colon tissue sample as compared to the control colon sample indicates that the patient has colon cancer.

The Office alleges that undue experimentation would be required for a person skilled in the art to practice the claimed invention. The Office notes that "if a molecule ... is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule." The Office also alleges that the Eid et al. reference:

> *clearly* teaches an example that demonstrates elevated levels of nucleotide sequences comprising SEQ ID NO:167 are found in prostate tissue samples from patients with prostate cancer as compared to levels of said sequences in non-cancerous prostate tissue samples. ... [and] that [t]he art does not hint or suggest that a decrease in expression of nucleotide sequences comprising SEQ ID NO:167 in prostate tissue samples, as compared to any type of control, would predictably indicate that the patient has prostate cancer"

(Office Action, page 16; emphasis in original). Applicants do not agree as no undue experimentation would be required for a person of skill in the art to practice the presently claimed methods.

To practice the invention, the skilled artisan need only determine if the level of nucleotide sequences comprising SEQ ID NO:167 in colon tissue samples from patients samples is at least 50% lower than the level of said sequences in non-cancerous colon tissue samples. Patient samples with such lowered levels compared to non-cancerous colon samples are indicative of colon cancer

With respect to the Office's requirement that a disease state be identified in some way with the molecule, Applicants respectfully point out that this correlation has been provided. First, Applicants note that the application as filed correlates Egr1 misexpression with cancer.

Other references support the correlation of down-regulation of Egr1 with colon cancer and provide the disease state-molecule link requested by the Office.

For example, Tice et al. (J. Biol. Chem., 2002, February 22, 277. 8:6118-6123) notes that Egr-1 expression is decreased in 9 out of 12 tumor samples from patients with colon cancer as compared to a non-cancerous control. A study published in 2005 by Jens Karsten Haberman confirms that gene expression levels of EGR1 are significantly reduced in colorectal cancer as compared to control (see, for example, page 57). Copies of the references cited above were included in a supplemental IDS filed concurrently with Applicants' June 27, 2007 response.

Measurement and comparison of levels of nucleotide sequences comprising SEQ ID NO:167, or full complements, thereof would not require undue experimentation, given the knowledge of one of skill. Accordingly, one skilled in the art would understand that any experimentation, if required, would be very amenable to automation. Applicants also remind the Office that in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), the court discussed the adequacy of disclosure with regard to a patent disclosing an immunoassay method for the detection of hepatitis B antigen using monoclonal antibodies. The *Wands* Court noted that of 143 hybridomas produced, only nine were assayed and, of those, only four hybridomas secreted IgM antibodies and exhibited a binding affinity constant for the HBsAg determinants of at least 10^9 M^{-1}, a "respectable 44 percent rate of success." *In re Wands*, 8 USPQ2d at 1406. Finding the claims were enabled, the Wands Court stated:

> Wands' disclosure provides considerable direction and guidance on how to practice their invention and presents working examples. There was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known.
>
> The nature of monoclonal antibody technology is that it involves screening hybridomas to determine which ones secrete antibody with desired characteristics. Practitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody. No evidence was presented by either party on how many hybridomas would be viewed by those in the art as requiring undue experimentation to screen.

In re Wands, 8 USPQ2d at 1406 (emphasis added). Therefore, where the art typically engages in a complex, but routine degree of experimentation, having to do so is not the undue experimentation proscribed by 35 U.S.C. § 112, first paragraph, under the reasoning of *In re Wands*. Even assuming, *arguendo*, that performing experiments to confirm the correlation reported by Applicants between increased expression of SEQ ID NO: 167 and colon cancer is considered "complex" (Applicants respectfully assert that any such experimentation would not be "complex"), Applicants submit that this kind of experimentation would be routine in the art, and therefore, does not constitute undue experimentation.

In view of the foregoing, Applicants respectfully requests withdrawal of the enablement rejection.

Claim Objections

Claims 29 and 36 were objected to for allegedly failing to further limit the subject matter of the claims on which they depend. Claim 36 was cancelled without prejudice, rendering the objection moot to the extent it applies to claim 36.

Claim 29 further limits that subject matter of claims 24 and 27. Claims 24 and 27 recite methods for determining whether a patient has colon cancer: decreased expression (by at least 50%) of nucleotide sequences comprising SEQ ID NO:167 in the patient tissue sample as compared to the patient control sample is indicative of colon cancer. Claim 29 is narrower in scope than either of claims 24 or 27, specifying that colon cancer is indicated when decreased expression (by at least 100%) of nucleotide sequences comprising SEQ ID NO:167 in the patient tissue sample as compared to the patient control sample is indicative of colon cancer. Because a method that would infringe claims 24 or 27 would not necessarily infringe claim 29 (for example, decreased expression of nucleotide sequences comprising SEQ ID NO:167 of 77% in the patient sample as compared to the control colon sample), claim 29 does further limit the subject matter of the claims from which it depends.

Accordingly, Applicants respectfully request the withdrawal of the objection to the claims.

Rejections under 35 U.S.C. §112, first paragraph (written description)

Claims 24, 25, 27, 29, 32, 33, 35 and 36 were rejected as allegedly failing to comply with the written description requirement. The Office alleges that although the application provides written description for sequences comprising SEQ ID NO:167 and the full complement thereof, written description is allegedly lacking for sequences at least 98% or at least 99% identical to SEQ ID NO:167 and a complement thereof. Applicants respectfully traverse.

Preliminarily, as set forth above, claims 25 and 32-36 were cancelled without prejudice. Claims 24 and 27 were revised to further clarify in which sample a decrease in expression levels is observed, to recite that the "complement" is a "full complement", and to recite a functional characteristic of the claimed sequences.

With respect to the Office's comments regarding 98% homologs, Applicants respectfully assert that adequate written description is provided in the application as filed. As discussed above, claim 24 was amended to specify that the 98% homolog encodes a polypeptide which binds to the promoter of the inosine-5'monophosphate dehydrogenase type II gene. Thus, the claimed sequences are defined by both sequence *and* function. In *Regents of the University of California v. Eli Lilly & Co.* 119 F.3d 1559 (Fed. Cir. 1997) the court stated that the written description requirement can be met by either a disclosure of a sufficient number of species within the claimed genus or a combination of structural and functional limitations. Thus, present claims 24, 25, 27, 29, 32, 33, 35 and 36 meet the standards set forth in *Lilly*.

In *Ex parte Sun* (Appeal No. 2003-1993; copy enclosed), the Board of Patent Appeals and Interferences considered the appropriateness of rejections under the written description and enablement requirements where the specification discloses a molecule within the claims and a functional assay for activity. The Board explained in *Ex parte Sun* that the following claim was illustrative of those on appeal.

> 31. An isolated wee1 nucleic acid molecule comprising a member selected from the group consisting of:
>
> (a) a polynucleotide that encodes a polypeptide of SEQ ID NO:2;

(b) a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1;

(c) a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1; and

(d) a polynucleotide complementary to a polynucleotide of (a) through (c).

The specification of the application on appeal disclosed that SEQ ID NO:2 encoded a protein having a defined function (similar to that of a known tyrosine kinase). The specification explained that the protein is useful in genetic engineering of corn plants to increase productivity. The examiner had rejected claim 31 as failing to meet the written description requirement, arguing that one skilled in the art could not predict the structure and function of nucleic acid "comprising a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1" The examiner had also argued that the specification did not "teach a single representative species with 80% identity and WEE1 function".

After reviewing the relevant case law, including *Lilly* and *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316 (Fed. Cir. 2002), the Board concluded that the rejected claims, including claim 31, met the written description requirement. The Board pointed out that the specification describes the sequence of a nucleic acid molecule encoding SEQ ID NO:2 and the sequence of a nucleic acid molecule comprising the coding sequence of SEQ ID NO:1. The Board also noted that the specification provides a description how to screen for WEE1 activity. The Board concluded that,

> [I]t would reasonably appear that such a description in the specification would constitute sufficiently detailed, relevant identifying characteristics of the claimed subject matter consistent with *Enzo*.
> In our view, the examiner has failed to indicate why one of ordinary skill in the art, who is in possession of the very specific chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, would be unable to recognize, upon reading the disclosure, that appellants invented the claimed subject matter, including homologues sharing structural features with the specifically claimed and disclosed structures.

In the present case, as in *Ex parte Sun*, a functional limitation is provided. One of skill in the art at the time the present application was filed would be able to determine whether sequences falling within the claimed genus satisfied the functional limitation, e.g. whether encoded polypeptides bind to the promoter of the inosine-5'monophosphate dehydrogenase type II gene. In *Ex parte Sun* the Board further concluded that the written description requirement was met even though only a single species is disclosed.

Accordingly, it is clear that the disclosure of even a *single* species combined with a functional assay provides an adequate written description for a claim to a genus of molecules. A person skilled in the art would recognize, upon reading the disclosure, that Applicants invented the claimed subject matter, including 98% homologs sharing structural features with the specifically claimed and disclosed sequences.

In view of the foregoing, Applicant respectfully requests withdrawal of the written description rejection.

New Matter

Claims 25 and 33 were rejected under 35 U.S.C §112, first paragraph as allegedly containing new matter. Claims 25 and 33 were cancelled without prejudice, thereby rendering the rejection moot.

Rejections Under 35 U.S.C. §102

Claims 35 and 36 stand rejected as allegedly anticipated by Eid et al. (Cancer Research 58, 2461-2468) as evidenced by Monia et al. (U.S. Patent 6,008,048). Although Applicants do not agree, claims 35 and 36 were cancelled without prejudice, thereby rendering the rejection moot.

July 27, 2007 Advisory Action

In the Advisory Action mailed July 27, 2007, the Office stated that:

> Amendments to claims 24 and 27 broadened the claimed subject method to one where a result indicates that a patient has colon cancer to a method wherein a result is indicative of, in every way, colon cancer. These amendments raise new 35 U.S.C. 112 first paragraph enablement issues, as they are now broadly drawn to methods comprising determining that an expression level is "indicative of', in every way, colon cancer. Further, these amendments raise possible art issues and would require further search

and that the amendments filed by Applicants fail to place the application in condition for allowance because:

> Amendments to claims 24 and 27 broadened the claimed subject method to one where a result indicates that a patient has colon cancer to a method wherein a result is indicative of, in every way, colon cancer. These amendments raise new 35 U.S.C. 112 first paragraph enablement issues, as they are now broadly drawn to methods comprising determining that an expression level is "indicative of', in every way, colon cancer.

Applicants do not agree. As set forth above, the claim language has been revised to recite that decreased expression levels of EGR1 in a patient sample as compared to a control indicate that the patient has colon cancer.

Conclusion

In view of the above, Applicants submit that the present application is in condition for allowance, and respectfully requests such a Notice. If the present application is not allowed and/or if one or more of the rejections is maintained or made final, Applicants hereby request a telephone conference with the Examiner and further requests that the Examiner contact the undersigned attorney at (302) 778-8458 to schedule a telephone conference.

Please apply any other charges or credits to Deposit Account 06 1050.

Respectfully submitted,

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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 27

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte YUEJIN SUN, BRIAN R. DILKES, BRIAN A. LARKINS, KEITH S. LOWE, WILLIAM J. GORDON-KAMM and RICARDO A. DANTE

Appeal No. 2003-1993
Application No. 09/470,526

ON BRIEF

Before WILLIAM F. SMITH, MILLS and GRIMES, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 2-11, 31, 33 and 35-36 which are the claims on appeal in this application. Claims 14, 32 and 37 have been allowed.

Claim 31 is illustrative of the claims on appeal and reads as follows:

31. An isolated wee1 nucleic acid comprising a member selected from the group consisting of:
(a) a polynucleotide that encodes a polypeptide of SEQ ID NO:2.;
(b) a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1;

(c) a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1; and
(d) a polynucleotide complementary to a polynucleotide of (a) through (c).

The prior art references relied upon by the examiner are:

Aligue et al. (Aligue), "Regulation of *Schizosaccharomyces pombe* Wee1 Tyrosine Kinase," J. Biol. Chem., Vol. 272, pp. 13320-13325 (1997)

Hemerly et al. (Hemerly), "Dominant negative mutants of the Cdc2 kinase uncouple cell division from iterative plant development," The EMBO Journal, Vol. 14, pp. 3925-3936 (1995)

Grounds of Rejection

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

These rejections are reversed.

DISCUSSION

In reaching our decision in this appeal, we have given consideration to the appellants' specification and claims, to the applied references, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the noted rejections, we make reference to the examiner's Answer for the examiner's reasoning in support of the rejection, and to the appellants' Brief for the appellants' arguments thereagainst. As a consequence of our review, we make the determinations which follow.

Background

The subject matter of the present application is generally directed to corn plant nucleic acids and their encoded proteins which are involved in cell cycle regulation. Specification, page 4. In particular, the claimed invention is directed to a wee1 homologue from maize, zmwee1, whose activity resembles related protein tyrosine kinases. Specification, page 6. The zmwee1 protein is indicated in the specification to be useful in the genetic engineering of the corn plant to increase maize productivity. Specification, page 3.

More specifically, claim 31 is directed to an isolated wee1 nucleic acid comprising a member selected from the group consisting of: a polynucleotide that encodes a polypeptide of SEQ ID NO:2.; a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1; a polynucleotide comprising the

coding sequence set forth in SEQ ID NO:1; and a polynucleotide complementary to a polynucleotide described above.

According to the prior art, Aligue, Wee1 tyrosine kinase regulates mitosis by carrying out the inhibitory tyrosine 15 phosphorylation of Cdc2 M-phase inducing kinase. Abstract. The specification confirms this, stating "induced wee1 overexpression results in phosphorylation of p34 at tyrosine-15 (inactivating p34), effectively blocking the transition from G2 into mitosis." Specification, page 37. The "encoded [wee1] protein is an important part of the checkpoint control machinery that regulates $p34^{cdc2}$ activity and it's [sic] participation in the active MPF (maturation promoting factor) complex." Specification, page 36. Wee1 activity can be stimulated by the CDK2-cyclin A complex, or inhibited by nim1. Specification, page 36.

Description

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

The Federal Circuit has discussed the application of the written description requirement of the first paragraph of § 112 to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court explained that

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus . . . [H]owever, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id.

The Lilly court also stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. at 1567, 43 USPQ2d at 1405. Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id. at 1568, 43 USPQ2d at 1406.

The Federal Circuit has also addressed the written description requirement in the context of DNA-related inventions. See Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'showing that an invention is complete by disclosure of **sufficiently detailed, relevant identifying characteristics** . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" [Emphasis added] Id. at 1324, 63 USPQ2d at 1613 .

The court in Enzo adopted its standard from the USPTO's Written Description Examination Guidelines. See 296 F.3d at 1324, 63 USPQ2d at 1613 (citing the Guidelines). The Guidelines apply to proteins as well as DNAs.

Finally, it is well-settled that the written description requirement of 35 U.S.C. § 112, first paragraph, can be satisfied without express or explicit disclosure of a later-claimed invention. See, e.g., In re Herschler, 591 F.2d 693, 700, 200 USPQ 711, 717 (CCPA 1979): "The claimed subject matter need not be described in haec verba to satisfy the description requirement. It is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented processes including

those limitations." (citations omitted). See also Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue.").

We apply the relevant law above to the facts before us. In the present case, the examiner argues that the "specification does not set forth what specific structural or physical features define the claimed isolated nucleic acids and transgenic cells, plants and seeds." Answer, page 4. The examiner argues that one skilled in the art "could not predict the structure and function of isolated nucleic acids comprising a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 or a polynucleotide complementary thereto, or cells, plants and seeds transformed therewith. The physical features of the claimed isolated nucleic acids and transgenic cells, plants, and seeds cannot be ascertained in the absence of information about the functional activities of these nucleic acids. Additionally, the specification does not disclose the effect of incorporating the claimed isolated nucleic acids into the genome of a cell or plant." Id.

We find the examiner's argument that one skilled in the art could not predict the structure and function of isolated nucleic acids comprising a wee1 to be confusing in the context of a written description rejection, as predictability is not the legal standard or test for such rejections. However, as best we can understand the examiner's argument, the examiner appears to argue that the specification does not describe a wee1

polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

The examiner argues that "Applicant's [sic] own specification fails to teach a single representative species with 80% identity and WEE1 function." Answer, page 5.

We do not agree with the examiner that claim 31 lacks written description in the specification and that appellants were not in possession of the claimed invention at the time the application was filed. First, to satisfy the written description requirement it is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented the claimed subject matter. Thus, we do not find the fact that the specification does not specifically teach the structure of a species with 80% identity and WEE1 function to be dispositive of the written description issue here.

The Enzo court stated that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" Id. at 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Contrary to the examiner's position, it would reasonably appear that such a description in the specification would constitute sufficiently detailed, relevant identifying characteristics of the claimed subject matter consistent with Enzo (*supra*).

In our view, the examiner has failed to indicate why one of ordinary skill in the art, who is in possession of the very specific chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, would be unable to recognize, upon reading the disclosure, that appellants invented the claimed subject matter, including homologues sharing structural features with the specifically claimed and disclosed structures.

The examiner relies on Aligue for the teaching that amino acids 363-408 of the 550 amino acid N-terminal regulatory domain of *S. pombe* WEE1 are critical to the function of the regulatory domain. The examiner concludes that because "the functional properties of WEE1 and other proteins reside in specific amino acid residues, changes in these residues could have an effect on WEE1 function." Answer, page 5.

We agree with appellants that the examiner has not established with a preponderance of the evidence, that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for wee1 activity and teachings of the areas of the wee1 gene that can be altered without disturbing substrate recognition are insufficient to describe a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. What is evident from the record is those of ordinary skill in the art were aware that most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. Those of skill in the art were also aware that the carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis. Thus, those of ordinary skill in the art would have recognized from reading the disclosure that the inventors had invented the isolated wee1 having the specific nucleotide and amino acid sequences and variations of these sequences with mutations in described specific areas of Wee1, while avoiding the introduction of mutations in other regions. This teaching, coupled with the ability to test for functional mutants with the assays provided for in the specification, supports appellants' position that the inventors sufficiently described and were in possession of the invention as claimed, at the time of filing of the patent application.

In our view the examiner has not provided sufficient evidence or analysis to indicate why one of ordinary skill in the art having read the disclosure, would not have been able to recognize that the inventors invented the subject matter within the scope of the claims. The rejection of the claims for lack of written description is reversed.

Enablement

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

It is the examiner's position that the specification is enabling for an isolated wee1 nucleic acid comprising a polynucleotide encoding SEQ ID NO:2 and a polynucleotide comprising SEQ ID NO:1, but does not reasonably provide enablement for a wee1 polynucleotide having 80% identity to the coding region of SEQ ID NO:1. Answer, page 6.

Enablement is a legal determination of whether a patent enables one skilled in the art to make and use the claimed invention, Raytheon Co. v. Roper Corp., 724 F.2d 951, 960, 220 USPQ 592, 599 (Fed. Cir. 1983), and is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive. Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984); W.L. Gore and Associates v. Garlock, Inc., 721 F.2d 1540, 1556, 220 USPQ 303, 315 (Fed. Cir. 1983). Nothing more than objective enablement is required, and therefore it is irrelevant

whether this teaching is provided through broad terminology or illustrative examples. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).

An analysis of whether the claims under appeal are supported by an enabling disclosure requires a determination of whether that disclosure contained sufficient information regarding the subject matter of the appealed claims as to enable one skilled in the pertinent art to make and use the claimed invention. In order to establish a prima facie case of lack of enablement, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. See In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). See also In re Morehouse, 545 F.2d 162, 192 USPQ 29 (CCPA 1976).

The threshold step in resolving this issue is to determine whether the examiner has met his burden of proof by advancing acceptable reasoning inconsistent with enablement. "Factors to be considered by the examiner in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman, [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." (footnote

omitted). In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988).

In the present case the examiner provided an analysis of several of the relevant enablement factors on pages 5-9 of the Answer. One of the examiner's primary arguments is that the specification does not disclose any specific structural or functional characteristics of any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. Answer, page 7. The examiner also argues that the "specification does not disclose any examples of how to make a transgenic host cell or plant comprising an isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1" or provide "any definitive evidence that introducing any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 into a plant will result in an alteration of the plant's phenotype." Id.

The examiner relies on Hemerly to support the position that the transformation of plant material is unpredictable in view of the disclosure. According to the examiner, Hemerly teaches "the transformation of *Arabidopsis* and tobacco plants with isolated nucleic acids encoding wild-type and mutant Cdc2a cell cycle regulatory proteins". Answer, page 8. Transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant designed to accelerate the cell cycle unexpectedly did not affect the development of transgenic plants. The transformation of *Arabidopsis* and tobacco with a Cdc2a mutant designed to arrest the cell cycle did affect the development of transgenic plants as expected. Id.

The examiner concludes (Id., pages 8-9)

> Given the unpredictability of determining the function of isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the unpredictability of altering the phenotype of a plant by transforming it with an isolated nucleic acid of SEQ ID NO:1 or isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the absence of guidance in the specification for making and using said nucleic acids and transgenic host cells, plants, and seeds, the lack of working examples, and given the breadth of the claims which encompass multiple polynucleotides having at least 80% identity to the entire coding region of SEQ ID NO:1, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.

Analysis of the enablement requirement in the present case dovetails with our analysis with respect to the written description requirement. In particular, the specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Brief, page 9. In addition, the specification page 3, lines 17-31, "describes the level of skill in the art as well as indicating areas of the wee1 gene that can be altered without disturbing substrate recognition." Brief, page 7. Moreover, the specification, page 3, states, "Most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. The carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis."

We agree with appellants that the examiner has not established that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for wee1 activity and teachings of the areas of the wee1 gene that can be altered without disturbing substrate recognition are insufficient to enable a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

Nor has the examiner established that one of ordinary skill in the art having the chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1 and the ability to test for expression as described in the specification, would be insufficient to transform cells, plants and seeds in view of the success described in the specification. While the examiner relies on Hemerly for the transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant, the examiner has not explained how or why potential unpredictability associated with Cdc2a expression is related to or affects Wee1 expression. Nor is it clear from the examiner's analysis that the examiner has fully considered the state of the art as it relates to the transformation of vectors, seeds and plant cells, as outlined in the specification.

The Patent and Trademark Office Board of Appeals stated:

> The test [for enablement] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Ex parte Jackson, 217 USPQ 804, 807 (1982).

In our view, upon reading the disclosure, those of ordinary skill in the art would have been provided a reasonable amount of guidance to make and use a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. The specification, pages 27-29 outlines methods for transfection and transformation of cells and the introduction of DNA into plants. The examples of the specification indicate successful expression of zmwee1 in E. coli as evidenced by the successful inhibition of cyclin-dependent protein kinase. Specification, pages 33-34. In view of the successful transformation of cells with the disclosed and claimed specific wee1, we find no evidence or sufficient indicated reason of record why one of ordinary skill in the art would not have had a reasonable expectation of success in transforming cells and plant cells with a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 without undue experimentation.

The rejection of the claims for lack of enablement is reversed.

CONCLUSION

The rejection of claims 2-11, 31, 33 and 35-36 under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention is reversed.

The rejection of claims 2-11, 31, 33 and 35-36 under 35 U.S.C. § 112, first paragraph for lack of enablement is reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED

WILLIAM F. SMITH Administrative Patent Judge	)
DEMETRA J. MILLS Administrative Patent Judge	) APPEALS AND
ERIC GRIMES Administrative Patent Judge	) INTERFERENCES

Appeal No. 2003-1993
Application No. 09/470,526

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